

**REMARKS**

Claims 92-164 will be pending after entry of the amendments herein. Claims 1, 2, 6, 7, 19, 53-57 and 75-91 are cancelled herein without prejudice or disclaimer and Applicant reserves the right to claim subject matter of the cancelled claims in one or more continuing patent applications. Claims 92-164 are new and find basis in the claims as originally filed and in specification throughout. Representative basis for the alleles specified in the new claims, and the association of the alleles with an increased risk or decreased risk of breast cancer, is in Table 19 on pages 96-97 and at paragraph 0055 on page 12, for example. The amendment to the specification herein also finds basis in Table 19, and described in greater detail hereafter. Accordingly, entry of the new claims and amendment to the specification will not introduce any prohibited new matter.

The Office rejected claims in the outstanding action for the following reasons summarized hereafter:

- i. Claims 1, 2, 6, 7, 19, 53-55, 75-80, and 82-91 were rejected under 35 U.S.C. 121, requiring an election of an invention to be examined;
- ii. Claims 1, 2, 19, 53, 55, 75 and 84 were rejected under 35 U.S.C. 112, first paragraph, for the specification allegedly lacking a written description;
- iii. Claims 1, 2, 6, 19, 53-55, 75, 76, 84 and 85 were rejected under 35 U.S.C. 112, first paragraph, for the specification allegedly lacking enablement to make or use the invention commensurate in scope;
- iv. Claims 1, 2, 6, 9, 53-55, 75-76 and 84-85 were rejected under 35 U.S.C. 112, first paragraph, for the specification allegedly lacking enablement by improperly incorporating by reference essential material described in the claimed invention;
- v. Claims 1, 2, 6, 19, 53-55, 75-76 and 84-85 were rejected under 35 U.S.C. 112, second paragraph, for allegedly failing to particularly point

out and distinctly claim the subject matter which applicant regards as the invention;

- vi. Claims 1, 6, 75 and 76 were rejected under 35 U.S.C. 102(b), for allegedly being anticipated by dbSNP rs1541998;
- vii. Claims 1, 2, 6, 19, 75 and 76 were rejected under 35 U.S.C. 103(a), for allegedly being unpatentable over rs1541998 in view of Soderlund (US Patent 6,013,431);

The claim amendments are introduced solely to expedite prosecution without prejudice or disclaimer of any previously claimed subject matter. Applicant has not dedicated or abandoned any unclaimed subject matter and has not acquiesced to any rejections or objections made by the Office by introducing the amendments. Applicant expressly reserves the right to pursue prosecution of any presently excluded or cancelled subject matter or embodiments in one or more future continuing patent applications. Remarks in response to the outstanding claim rejections are set forth hereafter.

#### Restriction and Election

Applicant elects subject matter of group I with traverse. Applicant notes the polymorphic position elected previously, position 23826 in SEQ ID NO: 2, corresponds to chromosome position 87330326. Independent claims 92 and 128, and several dependent claims, are generic to the elected subject matter. Applicant respectfully requests that the Office search and examine the full scope of the claims herein, and Applicant understands from the interview on May 14, 2008 the Office is willing.

#### Rejection for Alleged Lack of Written Description

The Office rejected claims 1, 2, 19, 53, 55, 75 and 84 for the specification allegedly lacking a written description of the claimed subject matter. The rejection respectfully is traversed and is moot given the rejected claims are cancelled herein without prejudice or disclaimer. The rejection is

inapplicable to the methods of claims 92-164 in view of the reasoning presented hereafter.

The specification provides an analysis of several polymorphisms in the MAPK10 locus of the human genome. Applicant identified the alleles specified in part (a) of claims 92 and 128 as significantly associated with an increased risk of breast cancer, and identified the alleles specified in part (b) of claims 92 and 128 as significantly associated with a decreased risk of breast cancer.

Table 19 on pages 96 to 97 of the specification, for example, clearly identifies several allelic variants significantly associated with increased risk of breast cancer, and counterpart allelic variants significantly associated with a decreased risk of breast cancer (p-value less than 0.05). For example, at position 13903 of SEQ ID NO: 2 the allelic frequency (AF) of allele A1 (guanine) and allele A2 (cytosine) are determined for the breast cancer “case” population and the “healthy” control population. For the cytosine allele (A2), the AF in the breast cancer population is 0.920 and the AF in the “healthy” population is 0.991. For the guanine allele (A1), the AF is readily inferred by subtracting the A2 AF from the integer 1 (A1’s AF = 1 - A2’s AF), as fully described in paragraph 0278 on page 96 of the specification. Therefore, the AF for the guanine allele (A1) is 0.080 in the breast cancer population and 0.009 for the “healthy” population, as summarized in the table hereafter.

Position 13903 of SEQ ID NO: 2	Breast Cancer Pool AF	Control Pool AF
A2 = C (cytosine)	0.920	<b>0.991</b>
A1 = G (guanine)	<b>0.080</b>	0.009

Thus, a cytosine corresponding to position 13903 of SEQ ID NO: 2 (the A1 allele) is associated with a decreased risk of breast cancer, as it is more prevalent in the “healthy” control population. And a guanine corresponding to position 13903 of SEQ ID NO: 2 (the A2 allele) is associated with an increased risk of breast cancer, as it is more prevalent in the breast cancer population. A

person of ordinary skill in the art also can detect the corresponding nucleotide on a complementary strand, as described in the specification at paragraph 0055 on page 12, for example.

By identifying the allele having a higher frequency in the breast cancer population and the allele having a higher frequency in the “healthy” population, Applicant identified, and had possession of, the allele associated with an increased risk of breast cancer and the allele associated with a decreased risk of breast cancer for each position designated by a p-value of less than 0.05. Accordingly, the specification provides a written description of the claimed subject matter consistent with 35 U.S.C. 112, first paragraph, and withdrawal of the rejection respectfully is requested.

#### Rejection for Alleged Lack of Enablement

The Office rejected claims 1, 2, 6, 19, 53-55, 75, 76, 84 and 85 for the specification allegedly lacking an enabling disclosure of the claimed subject matter. Applicant respectfully traverses the rejection and notes the rejection is due to the cancellation of the rejected claims without prejudice or disclaimer. The rejection is inapplicable to new claims 92-164 in view of the reasoning presented hereafter.

Applicant’s specification identifies alleles significantly associated with an increased risk or decreased risk of breast cancer, as addressed above. The specification shows each of these associations are made with a p-value of less than 0.05. These associations are shown by way of working examples in the specification, a relevant factor in the *In re Wands* decision cited by the Office. These factors, coupled with the high level of skill in the art for technology pertaining to the pending claims, leads to the conclusion that any experimentation associated with the full claim scope of claims 92 and 128 is routine and not undue. Accordingly, the specification provides an enabling disclosure of the claimed subject matter consistent with 35 U.S.C. 112, first paragraph, and Applicant respectfully requests withdrawal of the rejection.

Rejection for Alleged Lack of Enablement and Alleged Indefiniteness

The Office rejected claims 1, 2, 6, 9, 53-55, 75-76 and 84-85 for the specification allegedly lacking enablement by improperly incorporating by reference essential material described in the claimed invention. The Office also rejected claims 1, 2, 6, 9, 53-55, 75-76 and 84-85 for the specification allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejections respectfully are traversed, and are moot in view of the cancellation of the rejected claims without prejudice or disclaimer. The rejections are inapplicable to claims 92-164. The new claims do not include references to chromosome positions according to Build 33 of the GenBank database human genome sequence. Instead, the new claims reference positions within SEQ ID NO: 2 as the Examiner suggested during the telephonic interview of May 14, 2008. Applicant therefore respectfully requests withdrawal of these rejection under 35 U.S.C. 112, first and second paragraph.

Rejection for Alleged Anticipation and Obviousness

The Office rejected claims 1, 6, 75 and 76 under 35 U.S.C. 102(b) as they allegedly were anticipated by dbSNP rs1541998. The Office also rejected claims 1, 2, 6, 19, 75 and 76 under 35 U.S.C. 103(a) as they allegedly were unpatentable over rs1541998 in view of Soderlund (US Patent 6,013,431). The rejections are traversed and are rendered moot as the rejected claims are cancelled without prejudice or disclaimer.

New claims 92 and 128 clarify that increased or decreased risk of breast cancer is determined based on the presence of one or more particular alleles specified. The cited SNP database segment and Sodelund do not disclose, teach or suggest such methods. Applicant therefore respectfully requests withdrawal of the rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a).

### **CONCLUSIONS**

In view of the foregoing amendments and remarks, Applicant respectfully submits that the Office can properly withdraw the outstanding claim rejections and that the pending claims herein are in condition for allowance. Applicant therefore respectfully requests that the Office withdraw the outstanding claim rejections and issue a notice of allowance.

Applicant requests a telephone conference with the undersigned representative to expedite prosecution of this patent application. Applicant's representative can be contacted by telephone at (858) 623-3226.

In the unlikely event a fee calculation document or other pertinent document is separated from this submission and the Office determines that an extension and/or other relief is required, Applicant petitions for any required relief, including extensions of time, and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. **50-3473**.

Respectfully submitted,

Dated: June \*\*, 2008

By: /\*\*/

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